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Outcomes associated with early post-traumatic osteoarthritis and other negative health consequences 3–10 years following knee joint injury in youth sport

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Objective: Post-traumatic osteoarthritis (PTOA) commonly affects the knee joint. Although the risk of PTOA substantially increases post-joint injury, there is little research examining PTOA outcomes early in the period between joint injury and disease onset. Improved understanding of this interval would inform secondary prevention strategies aimed at preventing and/or delaying PTOA progression. This study examines the association between sport-related knee injury and outcomes related to development of PTOA, 3–10 years post-injury.
Design: This preliminary analysis of the first year of a historical cohort study includes 100 (15–26 years) individuals. Fifty with a sport-related intra-articular knee injury sustained 3–10 years previously and 50 uninjured age, sex and sport matched controls. The primary outcome was the 'Symptoms' sub-scale of the Knee Osteoarthritis and Injury Outcome Score (KOOS). Secondary outcomes included; the remaining KOOS subscales, body mass index (BMI), hip abductor/adductor and knee extensor/flexor strength, estimated aerobic capacity (VO_2max) and performance scores on three dynamic balance tests. Descriptive statistics (mean within-pair difference; 95% Confidence interval (CI) and conditional odds ratio (OR, 95% CI; BMI) were used to compare study groups.
Results: Injured participants demonstrated poorer KOOS outcomes [symptoms −9.4 (−13.6, −5.2), pain −4.0 (−6.8, −1.2), quality-of-life −8.0 (−11.0, −5.1), daily living −3.0 (−5.0, −1.1) and sport/recreation −6.9 (−9.9, −3.8)], were 3.75 times (95% CI 1.24, 11.3) more likely to be overweight/obese and had lower triple single leg hop scores compared to controls. No significant group differences existed for remaining balance scores, estimated VO_2max, hip or knee strength ratios or side-to-side difference in hip abductor/adductor or quadricep/hamstring strength.
Conclusions: This study provides preliminary evidence that youth/young adults following sport-related knee injury report more symptoms and poorer function, and are at greater risk of being overweight/obese 3–10 years post-injury compared to matched uninjured controls.

Introduction

Osteoarthritis (OA) is the most common chronic joint disease for which there is no known cure[1]. It is characterized by joint pain and mobility disability in the presence of radiographic changes (e.g., cartilage loss, joint space narrowing and osteophytes). Further, OA is linked with increased rates of comorbidity (e.g., obesity, diabetes and heart disease)[2], ranks 5th amongst all forms of disability world-

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wide[3] and is estimated to account for 85.5% of all societal costs related to arthritis[4].

While idiopathic OA typically develops in older adults, evidence suggests there is an increasing burden in youth and younger adults who develop post-traumatic osteoarthritis (PTOA) prematurely as a result of a joint injury sustained in their youth[5]. Although previous joint injury is associated with the onset of PTOA, the time course of symptom onset and etiology of the disease is complex and involves the consideration of multiple risk factors including individual predispositions (e.g., genetics) and lifestyle factors (e.g., overweight and obesity)[5–7]. Regardless, once sustained, an injury requires early diagnosis and care to ensure optimization of secondary preventative interventions that may slow disease onset and progression.

The sequence of events from joint injury to PTOA onset is particularly relevant to the knee joint as it is one of the most frequently injured joints during youth sport and recreation[8] and the joint most commonly affected by OA[1]. Specifically, sport and recreation participation has been identified as a leading cause of injury requiring medical attention amongst youth, with knee and ankle injuries being the most prevalent[9,10]. Further, prospective studies report that 12–20 years post knee injury, there is a 10-fold increased risk of developing knee OA (based on radiographic assessment), compared to an uninjured population[5]. In fact, more than 50% of individuals with an anterior cruciate ligament (ACL) tear or meniscus injury go on to develop PTOA[6,11].

In addition to pain, mobility disability and the potential for increased societal burden, knee joint injury has been shown to have physiological[12], functional[13,14], and behavioral[15] consequences that may have a detrimental influence on long-term health outcomes. There is, however, a paucity of research examining outcomes early (<10 years post-injury) in the period between joint injury and PTOA onset when secondary prevention interventions have the greatest potential to delay or prevent progression to disease[16]. Given the potential long-term health impact of joint injury, it is a priority to improve understanding of these injuries in youth and adolescent populations in the context of determining the origins of health and disease throughout the lifespan. Once joint injury has occurred, it is imperative that individuals who have yet to display clinical signs of PTOA but who are at high risk of developing the disease are studied as they may hold clues vital to the early detection, disease trajectory and development of interventions aimed at halting or slowing disease progression. The purpose of this research was to examine the association between a knee joint injury sustained in youth sport and early clinical (knee related symptoms and quality of life), structural (body mass index (BMI)), functional (strength, dynamic balance) and physiological (aerobic fitness) outcomes associated with early onset PTOA and other long-term health outcomes in the first 10 years post-injury.

Method

Study design

A preliminary analysis of an ongoing historical cohort study.

Participants

This preliminary analysis included 100 youth/young adults recruited into a historical cohort between June and December 2013. Fifty participants who had sustained a sport-related intra-articular knee injury 3–10 years previously and 50 uninjured age, sex and sport (at time of injury) matched controls. These participants represent the first 50 matched pairs recruited in year 1 (2013) of longitudinal historical cohort study (The Alberta Youth Prevention of Early OA Study) that will target recruitment of 100 matched pairs ($n = 200$) who will be followed annually for at least 3 years and will include a diversity of additional outcomes (e.g., imaging, biomarkers, biomechanics, healthcare utilization).

Participants were recruited by telephone contact after identifying them from one of three sources; previous cohort studies conducted by the Sport Injury Prevention Research Centre (SIPRC), University of Calgary that examined injury risk factors in various youth sports (both injured and uninjured participants)[17–22], the University of Calgary Sport Medicine Centre (SMC) database (injured participants only) or through personal distribution of study information by study co-investigators, collaborators and participants (uninjured controls only). The injured group included individuals who sustained an intra-articular knee injury during a previous cohort study (contact was attempted for all individuals from these previous studies that had sustained an intra-articular knee injury) or who had presented to the SMC with a sport-related intra-articular knee injury 3–10 years previously (contact was based on a computer generated random list). In contrast, the uninjured group included individuals who reported no time-loss knee injury, confirmed by medical consultation, in the previous 10 years. For the purposes of this study, intra-articular knee injury was defined as a clinical diagnosis of knee ligament, meniscal or other intra-articular tibio-femoral or patella-femoral injury (e.g., osteochondral, fractures *etc.*) within the past 3–10 years that required both medical consultation (physician or physiotherapist) and resulted in disruption of regular sport participation. Injury diagnoses were based upon diagnostic codes recorded on physical therapy completed injury report forms (for participants recruited from previous cohorts studies) and sport physician completed medical records (for participants recruited from the SMC database) and then confirmed by participants. Exclusion criteria included pregnancy, non-steroidal anti-inflammatory use or cortisone injection within 3 months prior to testing, a musculoskeletal injury within the previous 3 months prior to testing that resulted in time loss (work, school or sport), diagnosis of other arthritides, or any current medical problem that prevented participation in the functional testing aspect of the study (e.g., neurological conditions). A sample size of 100 is a conservative estimate based on the ability to detect a clinically meaningful difference (eight points)[23] between study groups for the primary (KOOS symptoms sub-scale) outcome ($1\text{-}\beta = 0.8$, $\alpha = 0.05$, uninjured mean = 95, injured mean = 87, standard deviation of within pair differences = 18)[24] based on univariate analyses adjusted for a 15% drop-out rate over the course of the 3 year historical cohort study. Ethics approval was granted from the Conjoint Health Research Ethics Board at the University of Calgary, Canada and all participants provide signed consent/assent and completed a Physical Activity Readiness questionnaire (PAR-Q, 2002) prior to testing.

Data collection

All data were collected during one testing session at the University of Calgary SMC. After completing a study questionnaire that gathered demographic details, information about knee injury/surgery (including information regarding additional ipsilateral or contralateral knee and lower extremity injuries) and medical history, as well as the Knee Injury and Osteoarthritis Outcomes Score (KOOS)[25], participants rotated through testing stations that measured anthropometric details (height, weight), lower extremity isometric strength, dynamic balance and estimated VO_2max. BMI (kg/m^2) was calculated from measurements of participants' height (to the nearest 0.1 cm; shoes removed) and weight (to the nearest 0.1 kg) assessed using a medical scale and stadiometer (Model 402 KL, Pelstar, USA). Background, measurement properties, testing procedures and data reduction for the KOOS, hip and knee isometric strength, dynamic balance tests (triple single leg hop, TSLH; Star Excursion balance test, SEBT; and Unipedal dynamic balance, UPDB) and VO_2 max (mlO_2 kg^{-1}min^{-1}) values predicted from the Leger 20 m shuttle run can be found in Appendix 1.

Analyses

Statistical analyses were performed using STATA (v12.1, Collage Station, Texas, USA). Where appropriate, data were tested for normality (Shapiro–Wilk Test, alpha = 0.05) and homogeneity of variance to ensure appropriateness of parametric analyses. In the case of missing data the participant and their matched pair were removed from the specific analyses Available historical baseline (3–10 years previous) information on covariates at the time of recruitment into the original cohort study (e.g., age, sex, weight, height, BMI, sport) are reported for both study groups (means or proportions; 95% Confidence interval (CI) or, median; range) and the significance of any observed clinical differences discussed. Similarly, covariates (e.g., age, time since knee injury, other lower limb injury) at historical cohort study recruitment are summarized and rates of non-participation and losses to follow-up reported for both study groups. Baseline age, sex and sport of those who participated in the study were compared to those that did not.

To account for the matched design descriptive statistics (mean difference; 95% CI) of within pair differences for all outcomes were calculated. Conditional (matched design) logistic regression (odds ratio (OR), 95% CI) to used to assess the odds of being overweight or obese between study groups. Specifically, BMI was dichotomized as either healthy weight or overweight/obese. For participants under 20 years BMI was converted into age and sex-specific percentiles using US growth charts and then categorized according to age and sex specific cut-offs (healthy = 5th–85th percentile, overweight = 85th– 95th percentile, or obese >95th percentile)[26,27]. For older (≥20 years of age) participants, BMI categories were defined as normal (18.5–24.9 kg/m^2) overweight (25.0–29.9 kg/m^2) or obese (>30.0 kg/m^2)[28]. Finally, a Pearson's correlation coefficient (r) was used to explore the relationship between KOOS sub-scales and a preliminary multivariable linear regression model adjusted for clustering by pair (backwards selection) was used to better understand the role that BMI (continuous data) may have in the relationship between injury history and KOOS symptom score was performed.

Results

In order to recruit 100 participants to the historical cohort telephone contact was attempted for 1162 individuals. Of these 322 individuals were reached resulting in a participation rate of 31.1%. Approximately 22% of non-participation was due to a lack of interest while there was a small percentage of individuals that were either ineligible (2.2%) or could not be matched (6.4%). There was no difference in the proportion (%; 95% CI) of females [participants 39% (35.7, 41.5); non-participants 42% (32.2, 51.7)], age [(participants 21 (20.7, 21.9); non-participants 22 (21.8, 22.2)] or distribution of sport participation between those that participated in the study (n = 100) and those that did not (n = 222).

Sixty-two percent (33/50) of uninjured and 52% (26/50) of injured participants were recruited from previous SIPRC cohort studies. Historical (3–10 year) baseline characteristics of these 59 participants are summarized in Table I. Due to methodological differences in these previous studies, historical baseline height, weight and BMI were available for only 38 (17 uninjured and 21 injured) of these 59 participants. As values for these variables were not available for all 50 matched pairs, between group comparison was not undertaken. Participants came from a variety of sporting backgrounds (hockey, soccer, track and running, basketball, volleyball, skiing, football, dancing, rugby and baseball) with the majority having been soccer (32%) and hockey (32%) players.

Table I
Summary of available historical baseline characteristics (3–10 years previously)

Variable	Uninjured n = 33	Injured n = 26
Sex (% female)	42	42
Age (years)	14.4 (13.3, 15.4)	14.3 (13.6, 15.0)
Height (cm)*	167.5 (161, 174)	173.9 (169, 178)
Weight (kg)*	55.3 (47.6, 63.1)	67.4 (61.5, 73.2)
BMI (kg/m^2)*	19.3 (17.8, 20.8)	22.1 (20.9, 23.4)
Baseline to follow-up (years)	8.1 (6.8, 9.4)	6.9 (5.6, 8.2)

Values represent mean (95% CI) accept for sex.
* Based on 17 uninjured and 21 injured participants (data missing for 16 uninjured and five injured participants). Due to missing data, between group comparisons have not been made.

Covariates at baseline recruitment into the historical cohort for all participants (n = 100) are summarized in Table II. Forty-two percent of the historical cohort was female and the median age of participants was 22 years. The median age of injury for the injured study group was 15 years and the median time between injury and follow-up was 6.6 years. Twenty of the injured participants had Grade III ACL sprains, all of which were surgically reconstructed. A further nine had meniscal injuries, five of which underwent arthroscopic surgery. Four had other ligament injuries (first to third degree Medial Collateral Ligament and Lateral Collateral Ligament sprains, or first to second degree ACL or Posterior Cruciate Ligament sprains) while two participants sustained intra-articular fractures. The remaining fifteen fell into an 'other' diagnostic category, consisting of patella-femoral dislocations and subluxations.

Descriptive statistics for all outcomes by study group are summarized in Table III, while within pair differences are summarized in Table IV. Two pairs were excluded from the strength analyses (dynamometer battery malfunction) and one for the estimated VO_2max analyses (refused) due to missing data. Injured participants had higher BMI, and scored lower, indicating poorer outcome, on all five sub-scales of the KOOS with the largest between group differences in the 'symptoms' and 'knee related quality of life' subscales. Additionally, the injured group had a slightly lower performance score on the triple single leg hop test. In contrast, no between group differences existed for measures of strength (side-to-side difference or index leg hip and knee ratios), the remaining dynamic balance test scores or estimated VO_2max. After dichotomizing BMI, participants with a history of knee injury were 3.75 times (95% CI 1.24, 11.3) more likely to be classified as overweight/obese (unadjusted conditional OR).

Table II
Characteristics at time of recruitment into the historical cohort, 2013–14

Variable	Uninjured n = 50	Injured n = 50
Sex (% female, 95% CI)	42	42
Age at follow-up (yrs; median, range)	22 (15–26)	22 (16–26)
Baseline to follow-up (yrs; mean, 95% CI)	7.0 (4.7, 9.0)	6 (3.0, 10.0)
Age at injury (yrs; median, range)	n/a	15, (9–18)
Injury to follow-up (yrs; median, range)	n/a	6.6, (3–10)
Number with index knee surgery	0	27*
Number with contralateral knee injury	0	16
Number with contralateral knee surgery	0	8†
Number with index lower limb injury	5	5
Number with contralateral lower limb injury	8	4

* 20 of these were ACL reconstructions.
† Four of these were ACL reconstructions.

Table III
Summary of descriptive statistics by study group

Outcome		Uninjured $n = 50$	Injured $n = 50$
KOOS Sub-scales	Pain	100 (94.4–100)	94.4 (88.9–100)
	Symptoms	96.3 (92.9–96.4)	85.7 (78.6–92.9)
	ADL	100 (100–100)	99.3 (95.6–100)
	Sport/Rec	100 (97.2–100)	94.4 (83.3–97.2)
	QoL	100 (97.2–100)	91.7 (86.1–94.4)
$KOOS_5$ (lower score denotes better function)		0.6 (0.2–1.8)	2.4 (1.2–4.6)
BMI (kg/m^2)		23.4 (21.0–24.6)	25.1 (22.8–27.6)
Strength side-to-side differential ratio†	Hip abductors	1.0 (0.5–1.4)	1.0 (0.7–1.6)
	Hip adductors	1.0 (0.5–1.7)	1.1 (0.7–2.0)
	Quadriceps	1.0 (0.5–2.4)	1.0 (0.8–1.8)
	Hamstrings	1.0 (0.6–2.3)	1.0 (0.5–1.6)
Strength ratio*	Abductor/Adductor	1.4 (0.5–3.0)	1.5 (0.9–4.2)
	Quadriceps/Hamstrings	1.7 (0.6–3.3)	2.0 (0.6–4.1)
TSLH (% of leg length)		462 (289–621)	439 (184–563)
SEBT (cm accounting for leg length)		80 (66–93)	78 (64–89)
UPDB (seconds)		4.8 (2.5–15.7)	4.3 (2.3–18.0)
VO_2max (ml/kg^2)		46.4 (36.5–53.0)	46.4 (36.5–49.7)

Values represent median (range).
* Index leg.
† Index leg/non-index leg. ADL = function in daily living, QoL = knee related quality of life, VO_2max = estimated maximum voluntary oxygen uptake.

Table IV
Summary of descriptive statistics for pair differences

Outcome		Matched pair difference $n = 50$
KOOS Sub-scales	Pain	−4.0 (11.2) −6.8, −1.2*
	Symptoms	−9.4 (5.1) −13.6, −5.2*
	ADL	−3.0 (7.8) −5.0, −1.1*
	Sport/Rec	−6.9 (10.6) −9.9, −3.8*
	QoL	−8.0 (10.2) −11.0, −5.1*
$KOOS_5$ (lower score denotes better function)		2.3 (1.5) 1.3, 3.3*
BMI (kg/m^2)		2.1 (4.1) 0.9, 3.4*
Strength side-to-side differential ratio+	Hip abductors	0.05 (0.3) −0.04, 0.15
	Hip adductors	0.10 (0.4) −0.13, 0.22
	Quadricep	−0.06 (0.4) −0.17, 0.05
	Hamstrings	−0.10 (0.4) −0.22, 0.02
Strength ratio†	Abductor/Adductor	0.22 (0.8) −0.02, 0.46
	Quadricep/Hamstring	0.23 (0.9) −0.05, 0.52
TSLH (% of leg length)		−30.9 (82.3) −54.3, −7.6*
SEBT (cm accounting for leg length)		−1.2 (7.6) −2.2, −0.2
UPDB (seconds)		−1.0 (4.2) −3.4, 0.92
VO_2max (ml/kg^2)		−1.9 (10.5) −5.2, 1.4

Values represent mean pair difference = injured−uninjured (standard deviation) 95% CI. + Index leg/non-index leg.
* Difference is significantly different than zero (alpha = 0.05).
† Index leg.

The correlations between the five KOOS sub-scale scores are reported in Table V. The correlation between the KOOS 'symptoms' and 'knee related quality of life' subscales (the two with the largest between group differences) was 0.787. Finally, preliminary multi-variable linear regression revealed a significant relationship between injury history and KOOS symptoms sub-scale score with the $\beta_{\text{injury coefficient}}$ of −9.43 (95% CI; −13.65, −5.21) indicating that injured participants scored a mean of 9.43 points lower on the KOOS symptoms sub-scale than controls ($F = 20.13$, $P < 0.001$, $r^2 = 0.17$). This relationship was not influenced by BMI and BMI was thus eliminated from the model. However, as it is likely that the true effect of BMI will require a model that simultaneously considers time since injury the true nature of the influence of BMI on this relationship cannot be elucidated without a larger dataset and/or follow-up data.

Table V
Correlations (r)* between KOOS subscale scores

KOOS subscale	Pain	Symptoms	ADL	SR	QoL
Pain	1.00				
Symptoms	0.641	1.00			
ADL	0.480	0.803	1.00		
SR	0.696	0.772	0.775	1.00	
QoL	0.603	0.657	0.633	0.787	1.00

* Correlations are based upon Pearson's correlation coefficients, SR = activities in sport and recreation.

Discussion

The findings of this study suggest that youth/young adults who sustain a sport-related intra-articular knee injury experience more knee related symptoms, which impact their function in daily living and sport/recreational activities and reduce their knee related quality of life (as measured by the KOOS), within 3–10 years following the injury. Further, although they appear to have similar dynamic balance, estimated VO_2max and similar hip and knee strength as their age, sex and sport matched controls, injured participants have a higher BMI and are 3.75 times (95% CI 1.24, 11.3) more likely to be categorized as overweight/obese.

Clinical symptomology

Although the difference in scores on the five KOOS sub-scales (ranging from −3.0 on the function in daily living to −9.4 points on the symptoms sub-scale) are statistically significant at a 95% confidence level their clinical relevance is not immediately apparent. Collins *et al.*[23] report the minimal detectable changes for each subscale as; pain 6–6.1, symptoms 5–8.5, function in daily living 7–8, function in sport/recreation 5.8–12 and quality of life 7–7.2. Thus, it is likely that the between group differences for the symptoms, function in sport/recreation and knee related quality of life subscales are clinically relevant, while the differences on the remaining sub-scales may represent possible emerging trends that will need to be confirmed with longitudinal follow-up. Nevertheless, these findings are consistent with values from a similar population of college freshman (mean age 18 years) with self-reported history of knee ligament injury[24] and suggest that young adults with a history of intra-articular knee injury demonstrate clinical symptomology consistent with the onset and future development of PTOA.

The moderately high correlation between the symptoms and knee related quality of life subscales ($r = 0.787$) suggests that these two subscales may be capturing similar domains of self-report knee related injury outcome. Specifically, that in this population, knee related symptoms influence knee related quality of life. Although no previous literature comparing the correlation between KOOS subscales could be found several authors have compared the KOOS subscale scores to the SF-36 subscale scores. For instance Roos *et al.*[25] reported that the KOOS 'symptoms' and 'knee related quality of life' from 21 participants (18–46 years) about to undergo ACL reconstruction correlated most highly with the SF-36 physical functioning ($r = 0.29$) and general health ($r = 0.28$) respectively. Similarly, Salavati *et al.*[29] demonstrated the 'symptoms' and 'knee related quality of life' from 57 athletes (25.6 ± 3.4 years) 7.6 ± 2.2 months after ACL reconstruction correlated most highly with general health ($r = 0.49$) and social functioning ($r = 0.59$) respectively.

BMI

Although BMI does not directly measure visceral body adiposity (which is strongly associated with an increased cardiometabolic risk)[30], it is widely used as a surrogate measure of adiposity in large epidemiological studies due to ease of measurement and ability to predict long-term disease risk[31]. Specifically, increasing BMI category and obesity are highly associated with multiple morbidity, cardiovascular disease and type-2 diabetes mellitus which in turn are major causes of morbidity and mortality in the industrialized world[30]. Obesity is also associated with poorer functional movement[32] and is well established as a risk factor for OA[33].

While injured participants in this study demonstrated higher BMI it is difficult to know if the increase in BMI was a consequence of, or preceded, the joint injury. A recent longitudinal cohort study conducted in the Netherlands has shown that children (7.7–12 years of age) overweight by BMI and percent total body fat are at higher risk for lower extremity injuries compared to those of normal weight[34]. Therefore it is plausible that the injured study group was of higher BMI prior to their joint injury and in fact the increased BMI contributed to the risk of injury. Although we only have historical baseline data related to BMI for 38 of the participants (and unable to perform between group comparisons) our data would suggest that this may be the case and highlights the importance of considering the influence of BMI on PTOA related outcomes in future analyses. Regardless, of the temporal sequence, injured participants demonstrated a higher risk of being categorized as overweight/obese and as a result it is plausible that their risk of PTOA resulting from previous joint injury will be compounded by emerging weight gain (accelerate the rate at which injured participants progress to disease and the rate at which the disease itself progresses). These findings also suggest that individuals with a 3–10 year history of intra-articular knee injury may be at higher risk for other long-term health outcomes compared to those with no previous history of knee injury.

Strength, estimated VO_2max, dynamic balance

There were no clear differences in strength (other than slightly lower side-to-side difference in quadriceps strength), VO_2max or dynamic balance outcomes identified in this study. However, on closer examination were possible emerging trends for reduced performance scores on the TSLH and UPDB tests as well as reduced VO_2max. These parameters need to be confirmed with a longer periods of repeated longitudinal follow-up in a larger sample size.

Implications for early detection and secondary prevention

The findings of this investigation may have implications for early detection and secondary prevention strategies aimed at delaying/preventing the onset of PTOA for individuals that sustained a sport-related intra-articular knee injury in their youth (<18 years of age). For instance, self-reported knee symptoms, reduced function in sport/recreation and knee related quality of life may prove helpful in identifying individuals at risk of future PTOA specifically if including a measure of joint structure such as a Magnetic resonance imaging (MRI) outcome. Further, as obesity is a modifiable risk factor for PTOA and future negative health-outcomes, interventions aimed at individuals who have sustained an intra-articular knee injury focused on maintaining a healthy weight would seem appropriate. This approach of maintaining a healthy weight, as opposed to relying on subsequent weight-loss interventions, is supported by evidence highlighting the difficulty of sustaining and high cost of multi-component weight-loss programs[33]. However, success of secondary prevention programs focused on maintaining healthy weight would require additional information related to physical activity participation, nutrition and individual's beliefs associated with physical activity participation, injury and OA in this population.

Strengths and limitations

The strengths of this investigation include the matched design (age, sex and sport at the time of injury) and the confirmation of intra-articular knee joint injury by a physiotherapist or physician at the time of knee joint injury, which minimizes potential misclassification bias. These data are from the first 100 participants recruited in year 1 of an ongoing longitudinal cohort study that will involve 200 participants (100 with an injury history and 100 age, sex and sport matched controls) who will be followed up on a diverse number of outcomes (e.g., inflammatory biomarkers, MRI, radiography, dual X-ray absorptiometry, physical activity participation, nutrition, healthcare utilization, kinetics and kinematics *etc.*) in addition to what has been presented here, annually for 3 years. A larger sample size may facilitate multivariable analyses to consider potential confounding by history of other lower limb injuries, time since injury, knee injury type and surgical intervention, which was not possible in the current investigation. Accordingly, it is important to consider that the conclusions presented here are based upon univariate analyses and may alter when multiple covariates are taken into account. A further consideration is that although this investigation was only fully powered for the main outcome (KOOS symptoms sub-scale) a smaller than expected standard deviation of within pair differences (less than 18) for all KOOS subscales (see Table IV) has resulted in finding significant differences (paired t tests, $P < 0.001$) even after considering multiple comparisons (alpha = 0.05/5 subscale comparisons = 0.01). Finally it is important to consider that participants in this study represent an active youth sport population and as such findings may be limited in generalizability to less active youth.

Conclusion

This study provides preliminary evidence that young adults with a history of sport-related knee injury demonstrate greater clinical symptomology consistent with the onset and development of PTOA. This group is also at higher risk of being categorized as overweight/obese, which compounds PTOA risk, and increased risk of future poor health outcomes. Although only preliminary, these findings have the potential to inform early identification of individuals at risk of PTOA and development of secondary prevention strategies aimed at reducing the individual, societal, and economic health burden of joint injury and PTOA.

Author contributions

CAE, LJW and JLW were responsible for the conception and design of the study as well as obtaining funding. JLW and CAE coordinated the study and managed all aspects including collection and assembly of the data. ANA, CAE and JLW planned the analyses. JLW conducted all analyses and wrote the first draft of the manuscript. All authors had full access to the data and contributed to the interpretation of the findings, critical revision of the manuscript and approved the final manuscript.

Role of the funding source

The sponsors had no involvement with respect to design, collection or data, analyses, interpretation writing or submission.

Competing interests statement

JLW has a postdoctoral fellow clinician scientist salary award from Alberta Innovates Health Solutions and has received Travel awards from the Alberta Osteoarthritis Team and the Canadian Clinician Scientist Training Program for conference attendance.

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Appendix 1. Background, Measurement Properties, Testing Procedures and Data Reduction for Study Outcomes

The KOOS is a self-report measure designed to evaluate knee related symptoms and function in young active patients with knee injury and OA. It has been validated in different populations varying in age, disease duration and activity levels, including in individuals post-ACL reconstruction[25], knee arthroscopy[35] and with a history of meniscectomy (with and without OA)[36]. Further, it has been shown to have high test-retest reliability (ICC's ranging from 0.78 to 0.97)[37]. The KOOS consists of 42 items in five subscales: pain, other symptoms, function in daily living, function in sport and recreation, and knee-related quality of life. Each item was scored on a 5-point likert scale ranging from no problems to extreme problems. Sub-scale scores were then summed, and the total sub-scale score transformed to a 0–100 scale (higher scores indicating better outcome). Finally, similar to Frobell and colleagues[38] a mean of the five sub-scale scores ($KOOS_5$) was calculated.

Hip abductor, adductor, and knee extensor, flexor isometric strength (Nm/kg) was assessed using hand-held isometric dynamometry (Model 01163, Lafayette Instrument, USA). Participants performed one practice and three experimental trials (5 s maximal effort of pushing/pulling into an immovable strap) for all muscles, interspersed by a 15 s rest periods, with the peak value from the three trials recorded for analyses. Hip abduction and adduction strength were measured using methods originally described by Jaramillo *et al.*[39] (dynamometer placed 5 cm proximal to the knee joint and secured to the thigh with an immovable strap with participants in a side-lying position), which have been reported as highly reliable (peak force ICC: intra-session 0.97–0.98; inter-session 0.87–0.95)[40,41]. Knee extension strength was measured using methods described by Willams-Andrews *et al.*[42] and Bohannon *et al.*[43] (peak force ICC: intra-session 0.96–0.97). Specifically, with participants seated with hips and knees in 90° and 60° flexion respectively, the dynamometer was placed 5 cm proximal to the distal tip of the lateral malleoli on the anterior shin and secured to the leg with an immovable strap[44,45]. Finally, knee flexion strength was tested in a prone position with the knee in 60° flexion and the dynamometer placed 5 cm proximal to the distal tip of the lateral malleoli on the posterior aspect of the ankle, and secured to the leg with an immovable strap. The peak isometric strength (N) scores were converted to torque values (Nm; force $\times$ distance between joint line and dynamometer position) and normalized to body weight (Nm/kg) before side-to-side differential (ratio of the index/non-index leg scores expressed as a percentage) and hip adduction/abduction, knee flexion/extension strength ratios were calculated. For the purposes of this investigation, the index leg refers to the injured leg of the injured participants and corresponding leg of the matched control.

Dynamic Balance was assessed with the Triple Single-Leg Hop (TSLH), Star-Excursion Balance (SEBT) and Unipedal Dynamic Balance (UPDB) tests. The TSLH test is a performance-based measure that evaluates neuromuscular control, force generating capacity and leg confidence that has been validated and used in individuals with ACL injury[46,47]. Longitudinally, it has been shown to be moderately correlated to the Global Rating Scale ($r = 0.44$) and Lower Extremity Functional Scale ($r = 0.26$)[48], and has been hypothesized to be a useful tool to predict risk of future problems as a result of a previous knee injury[49]. After a practice trial each participant performed two trials of three consecutive single-leg hops with the goal of jumping as far as possible[50]. For a trial to be included, the landing had to be solid without excessive unbalanced movements or twisting of the foot. The maximum distance across trials was recorded for each leg and expressed as a percentage of leg length. The SEBT is a combined measure of postural control, strength, range of motion, and proprioceptive abilities. Previous studies have reported excellent test-retest reliability (ICC 0.82–0.87)[51,52], an ability to detect balance deficits in young adults with chronic ankle instability[53], and predict lower limb injuries in high school basketball players[52]. Participants stood on one leg in the centre of a grid, with hands on the pelvis, and reached with the non-stance leg as far as possible in anterior, posterolateral and posteromedial directions[52]. A trial was discarded and repeated if the participant failed to maintain unilateral stance, lifted or moved the stance foot from the grid, touched down with the reach foot, or failed to return the reach foot to the starting position. After a practice trial on each leg, three trials on each leg were completed with 15 s rests between trials. The maximal reach distance at the point where the most distal part of the foot extended to was measured and normalized for lower limb length. The UPDB test is a timed test performed on a high-density (50 kg/m^3) closed cell, foam pad (Airex Balance Pad®, L-group, St. Louis, MO) that has been found to be reliable in youth athletic populations[54]. Participants stood in the centre of a foam pad with hands on hips, closed their eyes and elevated the non-test foot from the pad to balance on the test leg as long as possible. The maximum stance time of three trials (15 s rests between trials) was recorded for each leg. Loss of balance was defined as removal of one hand from the hip, eyes opening, touching the foam pad or floor surface with the non-test foot, movement of the test foot or foam pad from its original position.

VO_2max (mlO_2 $kg^{-1}min^{-1}$) values predicted from the Leger 20 m shuttle run were used to estimate aerobic fitness[55]. This test is a valid predictor of maximal VO_2 uptake[55,56] and has been shown to have excellent test re-test relability in both youth ($r = 0.89$) and adult ($r = 0.95$) populations[55]. Participants ran back and forth over a 20-m distance to audio signals from an iPad (Apple Inc.) application (Beep test trainer, www.ifittest.com) beginning at a speed of 8.5 km/h that was increased every minute by 0.5 km/h. The test ended when the participant failed to reach the 20 m lines concurrently with the audio signals, on two consecutive occasions. VO_2max was predicted from the running speed on the last stage as per Green *et al.*[57].

References

1. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, *et al*. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380: 2163–96.
2. Suri P, Morgenroth DC, Hunter DJ. Epidemiology of osteoarthritis and associated comorbidities. PM R 2012;4:S10–9.
3. Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, *et al*. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2197–223.
4. Brown TD, Johnston RC, Saltzman CL, Marsh JL, Buckwalter JA. Posttraumatic osteoarthritis: a first estimate of incidence, prevalence, and burden of disease. J Orthop Trauma 2006;20: 739–44.
5. Roos E. Joint injury causes osteoarthrits in young adults. Cur Opin Rheumatol 2005;17:195–200.
6. Gelber A, Hochberg M, Mead L, Wang N, Wigley F, Klag M. Joint injury in young adults and risk for subsequent knee and hip osteoarthritis. Ann Intern Med 2000;133:321–8.
7. Coggon D, Reading I, Croft P, McLaren M, Barrett D, Cooper C. Knee osteoarthritis and obesity. Int J Obes Relat Metab Disord 2001;25:622–7.
8. Emery C, Meeuwisse W, McAllister J. Survey of sport participation and sport injury in Calgary and area high schools. Clin J Sport Med 2006;16:20–6.
9. Emery C. Risk factors for injury in child and adolescent sport: a systematic review. Clin J Sport Med 2003;13:256–68.
10. Misra A. Common sports injuries: incidence and average charges. In: Health and Human Services U Ed. Office of the Assistant Secretary for Planning and Evaluation:5, http://aspe.hhs.gov/health/reports/2014/SportsInjuries/ib_SportsInjuries.pdf;.
11. Lohmander L, Ostenberg A, Englund M, Roos E. High prevalence of knee osteoarthritis, pain, and functional limitations in female soccer players twelve years after anterior cruciate ligament injury. Arthritis Rheum 2004;50:3145–52.
12. Steding-Ehrenborg K, Heden B, Herbertsson P, Arheden H. A longitudinal study on cardiac effects of deconditioning and physical reconditioning using the anterior cruciate ligament injury as a model. Clin Physiol Funct Imaging 2013;33:423–30.
13. Magyar MO, Knoll Z, Kiss RM. Effect of medial meniscus tear and partial meniscectomy on balancing capacity in response to sudden unidirectional perturbation. J Electromyogr Kinesiol 2012;22:440–5.
14. Hart JM, Pietrosimone B, Hertel J, Ingersoll CD. Quadriceps activation following knee injuries: a systematic review. J Athl Train 2010;45:87–97.
15. Granito V. Athletic injury experience: a qualitative focus group approach. J Sport Behav 2001;24:63–81.
16. Chu CR, Williams AA, Coyle CH, Bowers ME. Early diagnosis to enable early treatment of pre-osteoarthritis. Arthritis Res Ther 2012;14:212.
17. Emery CA, Meeuwisse WH. Injury rates, risk factors, and mechanisms of injury in minor hockey. Am J Sports Med 2006;34:1960–9.
18. Emery CA, Meeuwisse WH. Risk factors for injury in indoor compared with outdoor adolescent soccer. Am J Sports Med 2006;34:1636–42.
19. Emery CA, Rose MS, McAllister JR, Meeuwisse WH. A prevention strategy to reduce the incidence of injury in high school basketball: a cluster randomized controlled trial. Clin J Sport Med 2007;17:17–24.
20. Emery CA, Meeuwisse WH, Hartmann SE. Evaluation of risk factors for injury in adolescent soccer: implementation and validation of an injury surveillance system. Am J Sports Med 2005;33:1882–91.
21. Emery CA, Meeuwisse WH. The effectiveness of a neuromuscular prevention strategy to reduce injuries in youth soccer: a cluster-randomised controlled trial. Br J Sports Med 2010;44: 555–62.
22. Emery CA, Kang J, Shrier I, Goulet C, Hagel BE, Benson BW, *et al*. Risk of injury associated with body checking among youth ice hockey players. JAMA 2010;303:2265–72.
23. Collins NJ, Misra D, Felson DT, Crossley KM, Roos EM. Measures of knee function: International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form, Knee Injury and Osteoarthritis Outcome Score (KOOS), Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS), Knee Outcome Survey Activities of Daily Living Scale (KOS-ADL), Lysholm Knee Scoring Scale, Oxford Knee Score (OKS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Activity Rating Scale (ARS), and Tegner Activity Score (TAS). Arthritis Care Res 2011;63(Suppl 11):S208–28.
24. Cameron KL, Thompson BS, Peck KY, Owens BD, Marshall SW, Svoboda SJ. Normative values for the KOOS and WOMAC in a young athletic population: history of knee ligament injury is associated with lower scores. Am J Sports Med 2013;41:582–9.
25. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee injury and osteoarthritis outcome score (KOOS): development of a self-administered outcome measure. J Orthop Sports Phys Ther 1998;28:88–96.
26. CDC. English version. In: Body Mass Index Percentile Calculator for Child and Teen 2014;Vol. 2014.
27. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ 2000;320:1240–3.
28. CDC. English version. In: Adult Body Mass Index Calculator 2014;Vol. 2014.
29. Salavati M, Akhbari B, Mohammadi F, Mazaheri M, Khorrami M. Knee injury and Osteoarthritis Outcome Score (KOOS); reliability and validity in competitive athletes after anterior cruciate ligament reconstruction. Osteoarthritis Cartilage 2011;19:406–10.
30. Goodwin K, Syme C, Abrahamowicz M, Leonard GT, Richer L, Perron M, *et al*. Routine clinical measures of adiposity as predictors of visceral fat in adolescence: a population-based magnetic resonance imaging study. PLoS One 2013;8: e79896.
31. Booth HP, Prevost AT, Gulliford MC. Impact of body mass index on prevalence of multimorbidity in primary care: cohort study. Fam Pract 2014;31:38–43.
32. Duncan MJ, Stanley M, Leddington Wright S. The association between functional movement and overweight and obesity in

British primary school children. BMC Sports Sci Med Rehabil 2013;5:11.
33. Wluka AE, Lombard CB, Cicuttini FM. Tackling obesity in knee osteoarthritis. Nat Rev Rheumatol 2013;9:225–35.
34. Jespersen E, Verhagen E, Holst R, Klakk H, Heidemann M, Rexen CT, *et al.* Total body fat percentage and body mass index and the association with lower extremity injuries in children: a 2.5-year longitudinal study. Br J Sports Med 2013;48(20):1497–502.
35. Roos EM, Roos HP, Ekdahl C, Lohmander LS. Knee injury and osteoarthritis outcome score (KOOS): Validation of a Swedish version. Scand J Med Sci Sports 1998;8:439–48.
36. Roos EM, Roos HP, Lohmander LS. WOMAC Osteoarthritis Index: additional dimensions for use in subjects with post-traumatic osteoarthritis of the knee. Western Ontarion and McMaster Universities. Osteoarthritis Cartilage 1999;7:216–21.
37. Roos E, Toksvig-Larsen S. Knee injury and osteoarthritis outcome score (KOOS): from joint injury to osteoarthritis. Health Qual Life Outcomes 2003;1:64.
38. Frobell RB, Roos EM, Roos HP, Ranstam J, Lohmander LS. A randomized trial of treatment for acute anterior cruciate ligament tears. N Engl J Med 2010;363:331–42.
39. Jaramillo J, Worrell TW, Ingersoll CD. Hip isometric strength following knee surgery. J Orthop Sports Phys Ther 1994;20:160–5.
40. Lloyd-Ireland ML, Willson JD, Ballantyne B, Davis I. Hip strength in females with and without patellofemoral pain. J Orthop Sports Phys Ther 2003;33:671–6.
41. Fenter P, Bellew JW, Pitts TA, Kay RE. Reliability of stabilised commercial dynamometers for measuring hip abduction strength: a pilot study. Br J Sports Med 2003;37:331–4.
42. Williams-Andrews AW, Thomas MW, Bohannon RW. Normative values for isometric muscle force measurements obtained with hand-held dynamometers. Phys Ther 1996;76:248–59.
43. Bohannon RW. Reference values for extremity muscle strength obtained by hand-held dynamometry from adults aged 20 to 79 years. Arch Phys Med Rehabil 1997;78:26–32.
44. Wikholm JB, Bohannon RW. Hand-held dynamometer measurements: tester strength makes a difference. J Orthop Sports Phys Ther 1991;13:191–8.
45. Kramer JF, Vaz MD, Vandervoort AA. Reliability of isometric hip abductor torques during examiner- and belt-resisted tests. J Gerontol 1991;46:M47–51.
46. Eastlack ME, Axe MJ, Snyder-Mackler L. Laxity, instability, and functional outcome after ACL injury: copers versus noncopers. Med Sci Sports Exerc 1999;31:210–5.
47. Fitzgerald GK, Axe MJ, Snyder-Mackler L. A decision making scheme for returning patients to high-level activity with nonoperative treatment after anterior cruciate ligament rupture. Knee Surg Sports Traumatol Arthrosc 2000;8:76–82.
48. Reid A, Birmingham TB, Stratford PW, Alcock GK, Griffin JR. Hop testing provides a reliable and valid outcome measure during rehabilitation after anterior cruciate ligament reconstruction. Phys Ther 2007;87:337–49.
49. Fitzgerald GK, Lephart SM, Hwang JH, Wainner MR. Hop tests as predictors of dynamic knee stabilitiy. J Orthop Sports Phys Ther 2001;31:588–97.
50. Moksnes H, Risberg M. Performance-based functional evaluation of non-operative and operative treatment after anterior cruciate ligament injury. Scand J Med Sci Sport 2009;19:345–55.
51. Kinzey SJ, Armstrong CW. The reliability of the star-excursion test in assessing dynamic balance. J Orthop Sports Phys Ther 1998;27:356–60.
52. Plisky PJ, Rauh MJ, Kaminski TW, Underwood FB. Star excursion balance test as a predictor of lower extremity injury in high school basketball players. J Orthop Sports Phys Ther 2006;36:911–9.
53. Olmstead LC, Carcia CR, Hertel J, Shultz SJ. Efficacy of the star excursion balance tests in detecting reach deficits in subjects with chronic ankle instability. J Athl Train 2002;37:501–6.
54. Emery C, Cassidy J, Klassen T, Rosychuk R, Rowe B. Development of a clinical static and dynamic standing balance measurement tool appropriate for use in adolescents. Phys Ther 2005;85:502–14.
55. Léger LA, Mercier D, Gadoury C, Lambert J. The multistage 20 metre shuttle run test for aerobic fitness. J Sports Sci 1988;6:93–101.
56. Ramsbottom R, Brewer J, Williams C. A progressive shuttle run test to estimate maximal oxygen uptake. Br J Sports Med 1988;22:141–4.
57. Green MS, Esco MR, Martin TD, Pritchett RC, McHugh AN, Williford HN. Cross validation of two 20-m shuttle-run tests for predicting VO_2max in female collegiate soccer players. J Strength Cond Res 2013;27:1520–8.